## REMARKS

In an Office Action mailed February 13, 2006, the Examiner rejected Claims 11-12 under 35 U.S.C. § 112, first paragraph for failing to comply with the written description and enablement requirements. In addition, Claim 11 was rejected under 35 U.S.C. § 102(b) as being anticipated by Nakamura S, *et al.*, "Progression of nephropathy in spontaneous diabetic rats is prevented by OPB-9195, a novel inhibitor of advanced glycation," Diabetes 46(5):895-899 (1997). Finally, Claim12 was rejected under 35 U.S.C. § 103 over Nakamura *et al.* in view of Sone H, *et al*, "Disease model: hyperinsulinemia and insulin resistance. Part B--polygenic and other animal models," Trends Mol. Med. 7(8):373-376 (2001).

The Applicants respond to each of the Examiner's rejections below. In view of the amendments noted above and the arguments presented herein, the Applicants respectfully request reconsideration of the merits of this application.

Rejections Under 35 U.S.C. § 112

The Examiner alleged that the specification failed to contain a sufficient written description of compounds that have an effect on diabetes and diabetic nephropathy. The Applicants, however, note that the claims are not directed to any particular compound, but are instead directed to methods of testing any such compounds by using the T2ND rat described in the above-identified application. Neither the above-identified application nor the claims recited therein are directed to any particular agent. If particular compounds were the subject of the above-identified application, then the claims would have been directed to a particular agent or class of agents. A skilled artisan using the methods of testing recited in the above-identified application, however, is free to discover, and therefore to obtain a patent, on new agents that modulate the signs and symptoms of diabetes and diabetic nephropathy.

In addition, the Applicants note that the T2DN is a single inbred strain that is reproducible because the animals are genetic twins. These animals therefore have a specific genetic constitution and specific physiological characteristics. As such, the only variation in response to any agent is environmental. Animal models, while limiting, are the only available means of screening agents for therapeutic effectiveness *in vivo* prior to clinical testing. Clinical testing, however, is within the province of the FDA, not the Patent Office.

Furthermore, the Applicants note that paragraph [0057] provides support for the agent or class of agents that may modulate the signs and symptoms of diabetes and diabetic nephropathy. The skilled artisan is familiar with angiotensin II receptor antagonist, converting enzyme inhibitors, TGF-$\beta$ antagonists and antibodies, growth factor inhibitors,

PPar receptor agonists, anti-hypertensive agents and insulin-sensitizing agents; therefore, the above-identified application does not need to teach the details of these agents as anti-hyperglycemic agents in animal models or humans.

Moreover, the Applicants note that since of the filing date of the above-identified application, the methods of testing recited therein have been used with a variety of different agents. The agents include insulin, glyburide (a sulfonylurea), deferitin and sevelamar (a phosphate binder). More importantly, the methods of testing have been used with XL784, an experimental drug from Exelixis (San Francisco, CA), which has now moved into clinical trials, based in part, on the results of the studies conducted in the T2DN model. The Applicants would be willing to supply this information to the Examiner if needed. As such, the T2DN rat is a model system for testing new drugs that target a reduction in diabetic nephropathy. Therefore, the Applicants respectfully request reconsideration of this rejection as applied to Claims 11-12.

The Examiner also alleged that the specification does not enable the skilled artisan to test the effects of compounds to treat symptoms associated with type II diabetes in general. While not agreeing with the Examiner's analysis, the Applicants amend Claims 11-12 to recite that the method of testing occurs in the T2DN, which is obtained by a cross between a Fawn Hooded (FHH) rat and a GK rat. The Applicants find support for this amendment in paragraphs [0033] to [0034]. The Applicants also believe that the above-identified application is sufficiently enabling to the skilled artisan with respect to the T2DN rat. Accordingly, the Applicants respectfully request reconsideration of this rejection as applied to Claims 11-12.

Rejection Under 35 U.S.C. § 102(b)

The Examiner alleged that Nakamura *et al.* anticipates the limitations of Claim 11. The Applicants, however, amend Claims 11-12 to recite that the rat model is obtained from a cross between a FHH rat and a GK rat. Nakamura *et al.* do not mention a rat model resulting from a cross between a FHH rat and a GK rat for studying the effect of an agent on diabetes and diabetic nephropathy. Instead, Nakamura *et al.* teach evaluating OPB-9195 in Otsuka Long-Evans Toliushima Fatty (OTLEFT) rat. Thus, the Applicants respectfully request reconsideration of this rejection as applied to Claims 11-12.

Rejection Under 35 U.S.C. § 103

The Examiner alleged that although Nakamura *et al.* do not teach using a genetically altered rat with symptoms of type 2 diabetes, but that it would have been obvious to the skilled artisan to create such a rat after reading Sone *et al.* The Applicants respectfully disagree.

First, and as noted above, Nakamura *et al.* fail to teach a combination of FHH and GK strains. In addition, the mouse of Sone *et al.* is a knockout mouse, meaning that it has a deletion for the insulin gene. In contrast, the rat disclosed in the above-identified application is a transgenic rat, not a knockout rat. As such, the rat disclosed in the above-identified application contains a full complement of genes, including the insulin gene. Therefore, the Applicants submit that neither Nakamura *et al.* nor Sone *et al.* teach, suggest or motivate the skilled artisan to cross the FHH rat and a GK rat to get resulting T2DN rat, which retains the insulin gene and exhibits the phenotypic characteristics of type 2 diabetes, including high blood glucose, proteinuria, focal glomerulosclerosis, expansion of mesangial matrix of the glomerulus, thickening of renal basement membranes, vascular hylanosis and nodular glomerulosclerosis.

In addition, the Applicants note that the two strains, the FHH rat and the GK rat, both lack the phenotype of the T2DN rat. Accordingly, it was neither known, nor contemplated that such a cross would result in the phenotype displayed by the T2DN rat.

The Examiner also alleged that Sone *et al.* is directed to clarifying or deciphering the pathophysiology of type 2 diabetes. The Applicants, however, note that the T2DN rat disclosed in the above-identified application is not directed toward clarifying the pathophysiology of the type 2 diabetes. Instead, any further genetic modifications to the T2DN rat would be directed toward further mimicking a hallmark phenotypic characteristic of diabetes -- high blood glucose with progressive development of nephropathy -- to test for compounds that prevent or attenuate these phenotypic characteristics. Thus, the Applicants respectfully request reconsideration of this rejection as applied to Claims 11-12.

Fees

No fee is believed due in connection with this submission. However, if a fee is due, in this or any subsequent response, please charge the fee to Deposit Account No. 17-0055.

Likewise, no extension of time is believed due, but should any extension be required in this or any subsequent response, please consider this to be a petition for the appropriate extension of time and a request to charge the petition fee due to the same Deposit Account.

Respectfully submitted,

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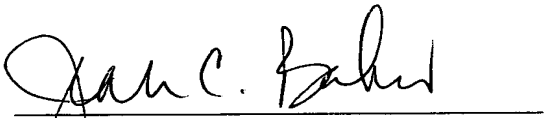

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